said targeted chromosomal material and detecting said bound probe, wherein bound probe is indicative of the presence of target chromosomal material.

49. The method of claim 48, wherein the target chromosomal material is interphase chromosomal material.

50. A method of staining targeted interphase chromosomal material based upon a nucleic acid segment employing a unique sequence high complexity nucleic acid probe of greater than about 50,000 bases, wherein said targeted interphase chromosomal material is a genetic rearrangement associated with chromosome 3 and/or chromosome 17 in humans, said method comprising contacting said interphase chromosomal material with a unique sequence high complexity nucleic acid probe of greater than about 50,000 bases, allowing said probe to bind to said targeted interphase chromosomal material and detecting said bound probe, wherein bound probe is indicative of the presence of target interphase chromosomal material.--

## REMARKS

Entry of the foregoing and reconsideration of the above-identified application as amended are respectfully requested. This amendment is believed to be consistent with 37 C.F.R. §1.116. Claim 1 was amended in view of the rejection under 35 U.S.C. §112. New claims 48-50 are added directed to preferred embodiments of the invention as recited in claim 1. No new search nor further consideration would be required by entry of this amendment.

Claim 1 has been amended to indicate that detection of bound probe is indicative of the presence of target chromosomal material. This makes clear that bound probe will only be detected when the targeted chromosomal material is present in the sample tested. Claim 1 has also been amended to recite that the probes are "about 50,000 bases." Support for this amendment may be in the recitation of "on the order of 50,000 (50 kb)" on page 44, line 7. Claims 48-50 have been added to recite further embodiments of the invention. In particular, claim 48 recites that the high complexity nucleic acid probe is greater than about 40 kb. Claims 49 and 50 specify that the target chromosomal material is interphase chromosomal material. Support for these claims may be found at the very least at page 45, lines 1-4, and page 121, lines 21-23, of the instant application, respectively. Support may similarly be found in the earliest filed application, i.e., Serial No. 06/819,314, filed January 16, 1986, at page 14, lines 18-21, and at page 37, lines 5-8, respectively.

Claim 1 has been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Examiner alleges that the phrase "high complexity nucleic acid probe" is vague and indefinite. According to the Examiner, the recitation in lines 2-3 of "probes" conflicted with the recitation in line 7 of "probe." The claim has been amended to correct this inconsistency and to recite "probe." The "high complexity nucleic acid probe" as claimed is believed to be sufficiently clear to a person of ordinary skill in the art. The size of the high complexity probe is recited in the claims as being greater than about 50 kb in claim 1 and about 40 kb in new claim 48.

The meaning of "high complexity nucleic acid probe" is further believed to be sufficiently clear upon review of the specification. For example, the specification states at page 42, lines 8-20:

> A probe is defined to be a collection of nucleic acid fragments whose hybridization to the target can be visualized. The probe is produced from some source of nucleic acid sequences, for example, a collection of clones or a collection of polymerase chain reaction (PCR) products. The source nucleic acid may then be processed in some way, for example, by removal of repetitive sequences or blocking them with unlabeled nucleic acid with complementary sequence, so that hybridization with the resulting probe produces staining of sufficient contrast on the target. Thus, the word probe may be used herein to refer not only to the detectable nucleic acid, but also to the detectable nucleic acid in the form in which it is applied to the target, for example, with the blocking nucleic acid, etc. The blocking nucleic acid may also be mentioned separately.

The specification further states at page 47, lines 14-25:

> One method of forming the probes of the present invention is to pool many different low complexity probes. Such a probe would then comprise a "heterogeneous mixture" of individual cloned sequences. The number of clones required depends no the extent of the target area and the capacity of the cloning vector. If the target is made up of several discrete, compact loci, that is, single spots at the limit of microscopic resolution, then about 40 kb, more preferably 100 kb, for each spot gives a reliable signal given current techniques. The portion of the probe for each spot may be made up from, for example, a single insert from a yeast artificial chromosome (YAC), from several cosmids each containing 35-40 kb or probe sequence, or from about 25 plasmids each with 4 kb of sequence.

Thus, the meaning of "high complexity nucleic acid probe" is believed to be clear to the skilled artisan when the claim is read in light of the specification. This aspect of the rejection should thus be withdrawn.

Claim 1 is also allegedly vague and indefinite in that the hybridization conditions are not defined in the claim. The claim recites a method of staining targeted chromosomal material based upon nucleic acid segment employing a unique sequence high complexity nucleic acid probe of greater than about 50,000 bases, wherein said targeted chromosomal material is a genetic rearrangement associated with chromosome 3 and/or chromosome 17 in humans, said method comprising contacting said chromosomal material with a unique sequence high complexity nucleic acid probe of greater than about 50,000 bases, allowing said probe to bind to said targeted chromosomal material and detecting said bound probe. The claim thus *requires* hybridization conditions wherein the probe binds to the targeted chromosomal material, if present, and is detected. The target is defined as being a genetic rearrangement associated with chromosome 3 and/or chromosome 17 in humans. The claim thus requires appropriate hybridization conditions such that the specified target, if present, is stained.

Such hybridization conditions are described in the application and need not be recited in the claim because the claims are read in light of the specification. Under 35 U.S.C. §112, second paragraph, a specification shall include claims "particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." Determining whether a claim is indefinite requires an analysis of "whether one skilled in

the art would understand the bounds of the claim when read in light of the specification.... If the claims read in light of the specification reasonably apprize those skilled in the art of the scope of the invention, [section] 112 demands no more." Credle v. Bond, 30 USPQ2d 1911, 1919 (Fed. Cir. 1994). In the instant application, this standard has been met.

Now turning to the prior art of record, claim 1 was rejected under 35 U.S.C. §103 as being unpatentable over Weissman et al. For at least the reasons set forth herein, this rejection is improper.

Weissman describes the spacing between genes including linkage that may be related to a disease. Weissman, however, fails to disclose or even suggest applicants' invention as now claimed. Weissman is unrelated to a method of staining targeted chromosomal material, wherein said targeted chromosomal material is a genetic rearrangement associated with chromosome 3 and/or chromosome 17 in humans. While Weissman describes spacing between and linkage of genes, Weissman is unrelated to detection of a genetic rearrangement in general, or more specifically one associated with chromosome 3 and/or chromosome 17 in humans. Nor does Weissman include any motivation to detect such chromosomal rearrangements using unique sequence probes as claimed. Instead, Weissman seeks to "determine the distance between, and/or orientation of two know genomic gene regions which are separated by a gene spacing of between about 20 and 2,000 kilobases" (col. 6, lines 55-59).

Weissman further fails to disclose or even suggest applicants' invention as recited in new claims 48-50. In particular, with respect to claims 49 and 50, Weissman fails

to disclose or even suggest a method of staining target *interphase* chromosomal material. By contrast, Weissman discloses only mapping to metaphase spreads (*see,* for example, Figure 5, Section VI and Example XI). That interphase chromosomal material could be reliably stained in a method as claimed is in no way taught by Weissman.

Withdrawal of this rejection as applied to the claims as amended is thus respectfully requested and believed to be in order.

Claim 1 of this application has also been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application Serial No. 08/487,701 and over claim 1 of Application Serial No. 08/478,387. Upon indication by the Examiner that claim 1 is otherwise in condition for allowance, applicants will consider filing a terminal disclaimer to overcome this rejection.

Regarding the objection to the disclosure in view of the recitation of "Related Applications," this objection is now moot in view of the instant amendment.

In view of the above, further and favorable action in the form of a Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this response, or to the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
Donna M. Meuth
Registration No. 36,607

Post Office Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: December 9, 1997